

Treatment of Arteriovenous Malformations with Hydrocoils in a Swine Model

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Summary

Arteriovenous malformations (AVM) of the brain are the most common symptomatic congenital vascular malformation of the central nervous system, with significant associated morbidity and mortality. This study compared the feasibility and efficacy of treating AVMs by embolization with hydrocoils with similar treatment with bare platinum coils, using the swine rete mirabile as a model. A right carotid–jugular fistula was created in ten swine. A microcatheter was positioned into the rete mirabile, which was unilaterally (contralateral to the fistula) embolized with hydrocoils in six and bare platinum coils in four swine. Angiograms were evaluated during and immediately after embolization. Embolization with complete cessation of blood flow in the unilateral rete mirabile was achieved in all animals treated with hydrocoils. The number of coils needed varied from four to seven (diameter 2–4 mm; mean coil length 22.3 cm). Embolization with platinum coils of similar number (seven) and slightly longer length (mean 37.75 cm) had a minimal effect on blood flow, resulting in occlusion of only small compartments. No immediate complications were noted with either coil. Hydrocoils are more effective in achieving embolization than bare platinum coils. Expansion of the hydrocoil over only a few minutes allows precise placement and

stabilization of the coil before detachment. Hydrocoils can be safely placed into small vessels. This approach may be particularly useful to decrease the flow rate, as a first stage of AVM embolization in high flow AVMs that contain arteriovenous fistulae.

Introduction

Arteriovenous malformations (AVM) of the brain are the most common symptomatic congenital vascular malformation of the central nervous system. Large-scale survey studies have suggested that the AVM detection rate is 1.21 per 100,000 person-years and the incidence of AVM hemorrhage is 0.42 per 100,000 person-years^{2,17,19}.

AVMs are associated with significant morbidity and mortality, with hemorrhage (43.4%), headache (24.9%), and seizure (17.3%) as the three most common neurologic manifestations²². AVMs are routinely treated by surgery, radiation therapy, and endovascular embolization or by a combination of these methods^{5,9,12,16}. Although the choice of approach remains the subject of debate in the literature, endovascular embolization is an increasingly common method for treating intracerebral AVMs^{4,18}. More than a decade ago, embolization was shown to be curative in 11.2% of endovascular cases²⁰. More recent studies have

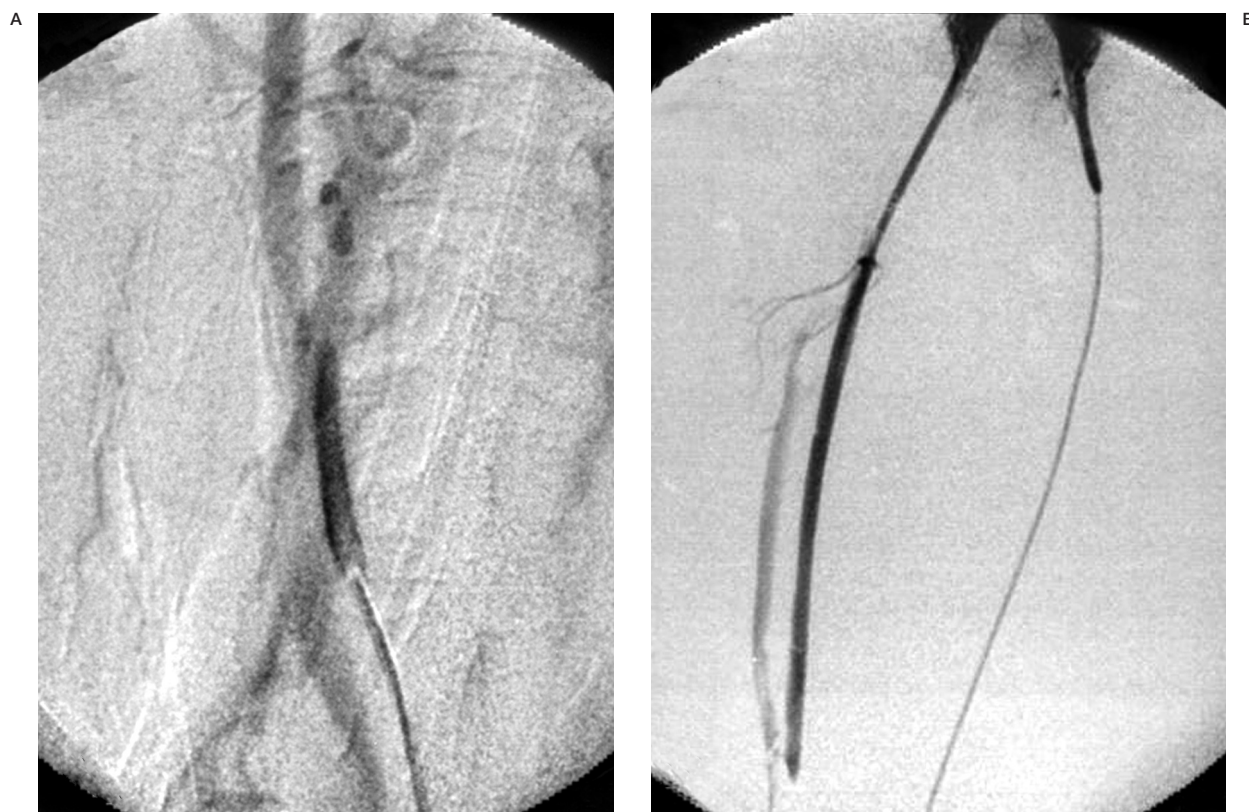


Figure 1 A,B Creation of carotid jugular fistula. A) Right carotid angiogram demonstrates filling of the jugular vein through created fistula. B) Filling across the rete mirabile during left carotid angiogram and retrograde filling of the right carotid artery and jugular vein.

indicated much higher success rates and low associated morbidity and mortality rates, as well as low complication rates with appropriate monitoring^{3,7,10,11}.

Among the greatest challenges in the embolization approach to AVM treatment has been the choice of embolic medium. N-butyl-2-cyanoacrylate (NBCA) is a fast-acting liquid adhesive polymer that has been proven to be an effective embolic medium in both animal models and patients^{20,21}. More recently, an ethylene vinyl alcohol copolymer (EVOH) preparation, ONYX, was introduced as a liquid embolic device¹. Precise placement of the embolic agent is challenging but is crucial in providing curative treatment and minimizing complications. An AVM can be treated completely and effectively if the embolic agent occludes the entire AVM nidus. Proximal occlusion of the feeding arteries without deep glue penetration, however, results in revascularization and regrowth of the AVM. The embolic agent must reach the proximal end of the venous compart-

ment adjacent to the AVM nidus, because collateralization in a partially occluded AVM may develop into the same initial draining veins. Obliteration of the AVM draining veins at early stages of embolization will result in increased intranidal pressure, which can increase the risk of swelling and hemorrhage. In addition, the penetration of embolic material into the venous channels may result in pulmonary complications. One recent study indicated a 16% rate of adverse events when glue was used in embolizations. These events included extravasations, partial artery occlusions, transient thromboembolus, and glued catheter⁷.

The problems associated with liquid adhesive devices have been particularly challenging in the treatment of high-flow AVMs or AVMs containing direct arteriovenous fistula. Multiple approaches were used to decrease the flow within the AVM prior to utilizing liquid embolic material. These devices include flow-directed (liquid injectable) coils and bare platinum detachable coils. Placement of injectable coils is

less predictable, and some coils end up crossing the AVM completely, with distal displacement into AVM draining veins or pulmonary vessels. Although placement of bare platinum detachable coils is more precise, the small volume of these coils may result in little change in flow. An approach that would allow precise placement, decrease flow within the AVM, and provide adequate and complete embolization would be optimal.

The Hydrocoil Embolic System (HES) (MicroVention, Inc.; Aliso Viejo, CA), introduced to clinical use in 2003, has been reported to compare favorably with platinum coils in aneurysm packing⁶. The HES is a platinum helical coil covered with a thin outer layer of a hydrogel polymer. Exposure to blood causes the hydrogel to expand to a predetermined diameter, achieving volumetric dimensions up to 11 times of comparable platinum coils in approximately 20 minutes. Short-term delayed expansion of the hydrocoil allows for precise distal placement and stabilization of the coil before detachment, with the potential for decreasing complications caused by glue. Moreover, the expanded hydrogel remains soft and conformable, providing a stable and permanent platform for blood stasis and thrombus remodeling.

Our study investigated the hypothesis that the hydrocoil can be used as an adjunct to other embolization devices in treatment of cerebral AVMs and was carried out in an established and well-verified swine AVM model (rete mirabile)¹⁴.

Methods

The study was approved by the participating center's institutional review board/ethics committee, and animals were handled in compliance with our dedicated animal research facility's regulations on the humane care and use of laboratory animals. Ten Yorkshire swine (weight, 30-40 kg) were obtained through our animal facility and included in the study.

Sedation

Each animal was sedated with intramuscular administration of Telazol (4.4 mg/kg) and xylazine (2.2 mg/kg). After the onset of sedation, general anesthesia was induced with 2%–4% isoflurane, followed by orotracheal intubation. Anesthesia was maintained with 1%–3% isoflurane, and the animal was ventilated. Intra-

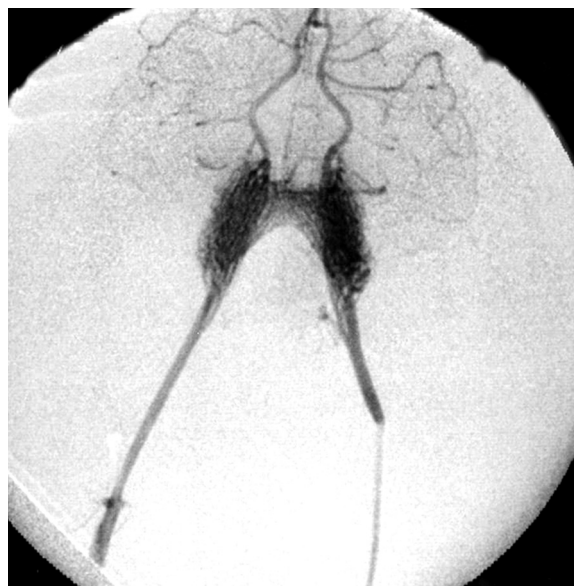


Figure 2 Rete mirabile angiogram.

operative monitoring was performed by veterinary staff and included continuous electrocardiography, pulse oximetry, and temperature monitoring.



Figure 3 Hydrocoil placement in the rete mirabile; contrast injection after first hydrocoil placement demonstrates filling defect within distal left lateral rete compartment due to occlusion by coils (arrows).



Figure 4 A-C Embolization with hydrocoils. A) Pre-embolization. B) Embolization in progress. Angiogram (contrast injection through microcatheter) demonstrates non-filling of the lateral aspect of the rete mirabile on the left after placement of three hydrocoils (arrows). C) Post-embolization. No residual filling. Coil artifact in the projection of the left rete mirabile.

Surgical Fistula Formation

The surgical preparation was similar to that described by Massoud et Al.¹⁹ in their original description of the creation of an AVM swine model. In addition, a carotid–jugular fistula was created on the side opposite to the embolization (figure 1). One side of the neck (usually the right) was shaved and scrubbed with three alternating scrubs of betadine and 70% alcohol and then draped. Sterile conditions and precautions were maintained throughout the procedure.

A ten cm incision was made in the neck, parallel to the sternocleidomastoid muscle. Self-retaining retractors were used to facilitate exposure, reflecting sternocleidomastoid muscle medially. A three cm segment of external jugular vein, free of tributaries, was dissected, isolated, and cleaned of adventitia. A three cm adjacent segment of the common carotid artery was also dissected, isolated, and cleaned of adventitia. Vasoconstriction, sometimes caused by handling of the artery and vein, was relieved by topical application of papaverine hydrochloride. Four small vascular clamps were placed at each end of the isolated common carotid artery and external jugular vein segments to achieve temporary occlusion during fistula creation. Microscissors were used to perform opposing elliptical arteriotomy and venotomy. The posterior margins of these were approximated and anastomosed using a continuous 7-0 prolene suture. After washing the vessel lumens with heparinized saline, the anterior margins were anastomosed similarly to form a side-to-side arteriovenous fistula. The vascular clamps were removed, and the right common carotid artery caudad to the fistula

was ligated. Subcutaneous tissue and skin were sutured as separate layers with 3-0 vicryl and 4-0 nylon, respectively.

Baseline Angiography

The animal's right groin was surgically prepared as described previously for the neck. The femoral artery was punctured with a Seldinger needle, which was exchanged for a 5-Fr sheath over Bentson wire. A 5-Fr guided catheter was used to select bilateral common carotid arteries for angiography of the rete mirabile in antero-posterior and lateral views utilizing a C-arm (used solely for animal research). During angiography, iodinated contrast (approximately 6–8 mL) was injected into the common carotid artery to outline normal anatomy of the rete mirabile (figure 2).

Embolization

An Excelsior microcatheter (Boston Scientific, Boston, MA) over microwire was placed through the guide catheter. The tip of the microcatheter was manipulated into as many distal branches of the rete mirabile vessels as possible under direct fluoroscopic guidance, and each branch was occluded utilizing hydrocoils in six and bare platinum coils in four animals. Hydrocoils were deposited to fill most of the rete mirabile volume. Initially, most distal compartments of the rete were targeted for embolization (figure 3). Similar numbers of coils were used in each animal embolized with bare platinum coils, and the same placement approach was used. Control angiograms were performed during the procedure to monitor the progress of embolization. Approximately 100 cc of contrast were used in each case. After microcatheter removal and embolization of the rete mirabile, final angiography was performed through the guided catheter positioned within the common carotid artery.

While animals were still under general anesthesia, euthanasia was performed with 100 mg/kg pentobarbital by intravenous bolus. The extent of rete mirabile embolization based on angiographic findings in the two types of coils was evaluated and compared.

Results

Completeness of embolization was defined as absolute cessation of blood flow in the unilateral rete mirabile as demonstrated on post-



Figure 5 Embolization with bare platinum coils. A) Pre-embolization. B) Postembolization. After placement of seven bare platinum coils, focal area of filling defect within mid/inferior portion of the left rete mirabile (arrows). No significant change in flow through the rest of the rete mirabile.

procedural angiography (figure 4). Complete embolization was achieved in all animals treated with hydrocoils. The number of coils needed for complete embolization in individual rete mirabilis ranged from four seven (diameter range, 2–4 mm; mean coil length, 22.3 cm) (table 1). No immediate complications were noted.

Only minimal embolic effects were seen in the animals treated with the bare platinum coils. In each animal, seven coils were used (the maximum number of coils used in hydrocoil experiments) with similar diameter and longer coil length (mean = 37.75 cm). The result in each animal was incomplete embolization of the rete mirabile with occlusion of only small compartments (figure 5).

Discussion

Intracerebral AVMs are managed today by multidisciplinary, multimodality treatment approaches. AVMs can be treated by microsurgery, endovascular embolization, stereotactic radiosurgery, or by a combination of these methods. Treatment planning depends on size, location, vascular architecture, flow dynamics, and clinical presentation of the AVM. Endovascular embolization is performed to completely and effectively treat the lesion or as a part of a combination treatment. Partial embolization may be performed preoperatively to decrease the rate of flow and hemorrhagic complications during microsurgery; in other cases it may be performed to decrease the flow and size of the nidus before radiation therapy. Sometimes the goal is to partially embolize otherwise untreatable brain AVMs.

Each of these procedures is associated with a significant risk of complications. Recent reports demonstrate mortality rates ranging from 1.1%–3.7% and morbidity rates ranging from 3.8%–14%¹⁰. Complications related to endovascular treatment include ischemic or hemorrhagic stroke leading to transitory or permanent neurologic deficits or to death. Significant factors associated with embolization-related complications include high-flow AVM, as a result of an arteriovenous fistula within the AVM nidus or a malformation purely composed of an arteriovenous fistula. A pure arteriovenous fistula is a direct communication between the artery and vein, without a plexiform nidus. This architecture facilitates the passage of embolic material to the venous side of the lesion, resulting in venous congestion, AVM rupture, and, possibly, symptomatic pulmonary embolism. A number of studies have noted devastating complications, including death, during embolization of high flow AVMs^{8,10,15}. In these difficult cases, multiple modifications to standard embolization technique were suggested, including flow-

control techniques to decrease the flow within the AVM as a first step. Flow control may be obtained by placement of detachable coils or injection of flow-directed “liquid” coils before glue injection. Inflation of a balloon proximal to glue injection was also suggested¹³. Our experience with hydrocoils suggests that this device may be especially useful in the situation of high-flow AVMs, where the flow may be decreased by controlled, precise coil placement at the level of fistula formation. This facilitates stabilization in place by allowing the coil to swell over a few minutes, and thus could potentially prevent the major complication of passage to the venous side during injection of glue or ONYX.

Although the swine rete mirabile is an established and well accepted model for the study of embolic devices that may then be directly translated into human AVM treatment, a few limitations should be noted. One is the relative sizes of the human and swine vessels involved. The mean diameter of the rete mirabile microvessels is 154 μm , which is close to the diameter of vessels composing the nidus of human brain AVMs. But some of the cerebral AVMs vessels are significantly larger (up to a few millimeters in diameter). In addition, the flow rate within our model is low compared with high-flow brain AVMs, even after we created a carotid–jugular fistula to augment the flow. Our work suggests that hydrocoils will be especially useful in large-vessel, high-flow cerebral AVMs, but no natural animal model is available in which to prove this hypothesis. Based on our animal experiments and growing data supporting safe use of hydrocoils in different vascular malformations, including dural fistulas and cerebral aneurysms, we suggest that hydrocoils may have a value in cerebral AVM treatment.

Conclusions

Our results suggest that hydrocoils can be placed safely into small vessels and may be used for treatment of brain AVMs. The technical advantages of this approach include coil expansion over only a few minutes, which allows placement distally into the vessel before swelling, and coil stabilization before detachment, which facilitates precise occlusion and avoids distal displacement. In the event of suboptimal initial placement of the coil, the ability

to retrieve the coil from the AVM before detachment allows for repositioning and, in humans, could prevent serious complications. This provides a significant safety advantage over other occlusion approaches, such as flow-directed coils, calibrated particles, or liquid tissue adhesives. In this study, hydrocoils were signifi-

cantly more effective in vascular embolization than were bare platinum coils of similar lengths. These results suggest that hydrocoils could be helpful in brain AVM treatment as the initial agent to decrease flow rate within the high-flow AVMs that contain an arteriovenous fistula.

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